1652

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

KOCK et al.

Serial No. 09/701,586

Filed: November 30, 2000

For: POLY(ADP-RIBOSE) POLYMERASE-GENE

MAIL STOP PETITIONS

Art Unit: 1652

Examiner: Hudson

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on:

August 1, 2003
Date of Deposit

Herbert B. Keil
Person Making Deposit

Herbert B. Keil
Signature

August 1, 2003
Date of Signature

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

PETITION TO THE COMMISSIONER UNDER 37 CFR §1.144

Sir:

Applicants hereby petition to the Honorable Commissioner to review the final restriction requirement in the above-indicated application, dated January 13, 2003.

STATEMENT OF MATERIAL FACTS

1. This application is a US national stage application filed in the US on November 30, 2000, based on international application PCT/EP/99/03889, which was filed on June 4, 1999.

2. In a first office action dated September 24, 2002 (paper 11), the examiner divided claims 1-32 into fifteen groups, asserting lack of unity of invention, and requiring election of a single group for prosecution (pp. 2-3). The examiner additionally identified three sequence groups, two consisting entirely of part-sequence motifs and the third including all claimed sequences, and required selection of "one sequence for examination practice" (p.3-4).

3. Applicants filed a timely response to the restriction requirement on October 24, 2002 (paper 13). Applicants elected the group designated as Group I by the examiner with traverse, and reasons for the traversal of the restriction requirement were provided with applicants's response. As the examiner's remarks pertaining to the sequence groupings appeared to be an election of species requirement, applicants elected sequence 2 for examination search purposes, again with traverse.

4. In a first office action on the merits, dated January 13, 2003 (paper 14), the examiner maintained the requirement for restriction and made it final. The examiner further indicated that no election of species requirement had been made.

5. Applicants filed an amendment under 37 CFR §1.111 in response to the

issues on the merits in the examiner's first action, which amendment was filed on July 7, 2003 (paper 16).

STATUS OF THE CLAIMS

The claims pending in this application are claims 1-32. A copy of the pending claims as amended in applicants' amendment under 37 CFR §1.111 is found in the attached appendix.

REMARKS

The present application contains claims drawn to subject matter which is related in such a way that unity of invention is present. To find unity of invention among a group of inventions, the subject matter must form a single general inventive concept by exhibiting a technical relationship involving one or more of the same or corresponding special technical features, which features define the inventions' collective contribution over the prior art. This requirement is set forward in PCT Rule 13 and codified in 37 CFR §1.475.

In the first office action requiring restriction, the examiner appears to consider, and then dismiss, the "special technical feature" status of the subject matter of claims 1-4 (p.4). In doing so, the examiner states that

> the PARP homolog, which has a functional NAD^+ binding domain but no zinc finger sequence motif of the general formula $CX_2C[X]_mHX_2C$ is anticipated by Lepiniec et al. (FEBS 364:103-108, 1995). Thus, Groups I-XV lack a common special technical feature.

(p.4.) In their response, applicants amended claim 1 to require that the PARP homolog

comprise a functional NAD^+ binding domain with the sequence $PX_n(S/T)GX_3GKGIYFA$, which differs from that in the PARP homolog of Lepiniec.

The examiner, in turn, asserted that the amendment was insufficient to overcome the earlier argument, as a second reference, Johansson (Genomics 57, pp.442-445), disclosed such a PARP homolog (paper 14, p.2). However, as applicants have pointed out in their most recent response, Johansson is not prior art. The present priority dates precede those dates indicated as the "Received" and "Accepted" dates for the Johansson manuscript, as well as the date of actual publication.

Claim 1 was also rejected as anticipated by Thibodeau et al. (Biochem. Cell Biol. Vol.67, pp.653-660). However, this reference discloses only "the sequencing of a rat partial cDNA encoding the NAD binding domain of the poly(ADP-ribose) polymerase" (p.654). Thus, it discloses only a partial sequence of the rat PARP homolog, and does not anticipate the present claim. Accordingly, the subject matter of claim 1 is novel over the prior art, and the claimed PARP homolog is a special technical feature which defines the contribution of the present group of inventions over that art.

The technical relationship between the various groups of claims, based on this special technical feature, is also readily apparent. Group I (cl.1-4) is composed of claims to the novel PARP homolog itself. Groups V and VI (cl.6-11) are composed of claims to nucleic acid sequences encoding the novel PARP homologs and various compositions of matter necessary for expressing these sequences. As indicated in

Example 17 of the PCT Administrative Instructions, Annex B, Part 2 (MPEP pp.AI-60 to AI-61),

> Expression of the DNA sequence in a host results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between [these] claims ... is accepted.

Applying this example to the present claims, applicants respectfully submit that unity of invention is present between the subject matter of presently defined Group I and that of presently defined Groups V and VI. Accordingly, at a minimum, these groups should be examined together.

The subject matter of Groups II-IV and VII-XV likewise exhibit unity of invention with the PARP homologs of Group I. In each of these other groups, the special technical feature of Group I is related to the subject matter therein through a particular technical relationship. For instance, Groups II-IV contain claims drawn to binding partners for the PARP homologs of claim 1, and methods of using these binding partners to diagnose and treat pathological states involving PARP homologs. The technical relationship resides in the binding partners' ability to bind with the novel PARP homologs. The remaining groups contain claims which are also drawn to subject matter linked together by various technical relationships, each of which involves the novel PARP homolog. Accordingly, unity of invention is present for all of Groups, and the entire application should be examined at the present time.

CONCLUSION

In view of the foregoing remarks, it is urged that applicants's claims as presently pending meet the unity of invention requirement as set forth in PCT Rule 13 and 37 CFR §1.475 which is applicable in the present case under PCT Article 27. It is therefore requested that the examiner's restriction requirement be withdrawn and that the application be returned to the examiner for further examination. It is also respectfully solicited that any unfairness in the compensation of the examiner due to differences between US national restriction practice under 35 USC §121 and unity of invention provisions under the PCT be resolved internally at the USPTO.

A check in the amount of $130.00 to cover the required fee for this paper is attached.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,
KEIL & WEINKAUF

David C. Liechty
Reg. No. 48,692

1350 Connecticut Ave., N.W.
Washington, D.C. 20036
(202)659-0100
DCL/kas

APPENDIX

PRESENT CLAIMS AS AMENDED UNDER 37 CFR §1.111

1. (previously amended) An isolated and purified poly(ADP-ribose) polymerase (PARP) homolog having an amino acid sequence which

a) has a functional NAD^+ binding domain comprising the sequence motif
$PX_n(S/T)GX_3GKGIYFA$ (SEQ ID NO:11)
in which n is an integral value from 1 to 5, and the X radicals are, independently of one another, any amino acid;

and

b) lacks a zinc finger sequence motif of the general formula
$CX_2CX_mHX_2C$ (SEQ ID NO:30)
in which
m is an integral value of 28 or 30, and the X radicals are, independently of one another, any amino acid;

said PARP homolog being selected from the group consisting of human PARP2 (SEQ ID NO: 2), human PARP3 type 1 (SEQ ID NO:4), human PARP3 type 2 (SEQ ID NO:6), murine PARP long form (SEQ ID NO:8), murine PARP short form (SEQ ID NO:10), and functional equivalents thereof which are at least 85% homologous.

2. (previously amended) A PARP homolog as claimed in claim 1, wherein the functional NAD^+ binding domain comprises one of the following general sequence motifs:

$(S/T)XGLR(I/V)XPX_n(S/T)GX_3GKGIYFA$ (SEQ ID NO:12) or
$LLWHG(S/T)X_7IL(S/T)XGLR(I/V)XPX_n(S/T)GX_3GKGIYFAX_3SKSAXY$ (SEQ ID NO:13)

in which
n is an integral value from 1 to 5, and the X radicals are, independently of one another, any amino acid.

3. (previously amended) A PARP homolog as claimed in claim 1, comprising at least another one of the following part-sequence motifs:

$LX_9NX_2YX_2QLLX(D/E)X_{10/11}WGRVG$ (SEQ ID NO: 15),
$AX_3FXKX_4KTXNXWX_5FX_3PXK$ (SEQ ID NO:16),
$QXL(I/L)X_2IX_9MX_{10}PLGKLX_3QIX_6L$ (SEQ ID NO:17),
$FYTXIPHXFGX_3PP$ (SEQ ID NO:18); and

$KX_3LX_2LXDIEXAX_2L$ (SEQ ID NO:19),

in which the X radicals are, independently of one another, any amino acid.

4. (canceled)

5. (previously amended) A binding partner for PARP homologs as claimed in claim 1, selected from
   a) antibodies and fragments thereof,
   b) protein-like compounds which interact with a part-sequence of the protein, and
   c) low molecular weight effectors which modulate the catalytic PARP activity or another biological function of a PARP molecule.

6. (previously amended) A nucleic acid comprising
   a) a nucleotide sequence coding for at least one PARP homolog as claimed in claim 1, or the complementary nucleotide sequence thereof;
   b) a nucleotide sequence which hybridizes with a sequence as specified in a) under stringent conditions; or
   c) nucleotide sequences which are derived from the nucleotide sequences defined in a) and b) through the degeneracy of the genetic code.

7. (original) A nucleic acid as claimed in claim 6, comprising

   a) nucleotides +3 to +1715 shown in SEQ ID NO:1;
   b) nucleotides +242 to +1843 shown in SEQ ID NO:3;
   c) nucleotides +221 to +1843 shown in SEQ ID NO:5;
   d) nucleotides +112 to +1710 shown in SEQ ID NO:7; or
   e) nucleotides +1 to +1584 shown in SEQ ID NO:9.

8. (previously amended) An expression cassette comprising, under the genetic control of at least one regulatory nucleotide sequence, at least one nucleotide sequence as claimed in claim 6.

9. (original) A recombinant vector comprising at least one expression cassette as claimed in claim 8.

10. (original) A recombinant microorganism comprising at least one recombinant vector as claimed in claim 9.

11. (original) A transgenic mammal comprising a vector as claimed in claim 9.

12. (previously amended) A PARP-deficient mammal or PARP-deficient eukaryotic cell, in which functional expression of at least one gene which codes for a PARP homolog as claimed in claim 1 is inhibited.

13. (previously amended) An in vitro detection method for PARP inhibitors, which comprises

    a) incubating an unsupported or supported polyADP-ribosylatable target with a reaction mixture comprising
        a1) a PARP homolog as claimed in claim 1,
        a2) a PARP activator; and
        a3) a PARP inhibitor or an analyte in which at least one PARP inhibitor is suspected;
    b) carrying out the polyADP ribosylation reaction; and
    c) determining the polyADP ribosylation of the target qualitatively or quantitatively.

14. (original) A method as claimed in claim 13, wherein the PARP homolog is preincubated with the PARP activator and the PARP inhibitor or an analyte in which at least one PARP inhibitor is suspected, before the polyADP ribosylation reaction is carried out.

15. (original) A method as claimed in claim 13, wherein the polyADP-ribosylatable target is a histone protein.

16. (previously amended) A method as claimed claim 13, wherein the PARP activator is activated DNA.

17. (previously amended) A method as claimed in claim 13, wherein the polyADP ribosylation reaction is started by adding NAD^+.

18. (previously amended) A method as claimed in claim 13, wherein the polyADP ribosylation of the supported target is determined using anti-poly(ADP-ribose) antibodies.

19. (previously amended) A method as claimed in claim 13, wherein the unsupported target is labeled with an acceptor fluorophore.

20. (original) A method as claimed in claim 19, wherein the polyADP ribosylation of the unsupported target is determined using anti-poly(ADP-ribose) antibody which is labeled with a donor fluorophore which is able to transfer energy to the acceptor fluorophore.

21. (original) A method as claimed in claim 19, wherein the target is biotinylated histone, and the acceptor fluorophore is coupled thereto via avidin or streptavidin.

22. (previously amended) A method as claimed in claim 20, wherein the anti-poly(ADP-ribose) antibody carries a europium cryptate as donor fluorophore.

23. (previously amended) An in vitro screening method for binding partners for a PARP molecule, which comprises

a1) immobilizing at least one PARP homolog as claimed in claim 1 on a support;

b1) contacting the immobilized PARP homolog with an analyte in which at least one binding partner is suspected; and

c1) determining, where appropriate after an incubation period, analyte constituents bound to the immobilized PARP homolog;

or

a2) immobilizing on a support an analyte which comprises at least one possible binding partner for a PARP molecule;

b2) contacting the immobilized analyte with at least one PARP homolog as claimed in claim 1 for which a binding partner is sought; and

c2) examining the immobilized analyte, where appropriate after an incubation period, for binding of the PARP homolog.

24. (previously amended) A method for the qualitative or quantitative determination of nucleic acids encoding a PARP homolog as claimed in claim 1, which comprises

a) incubating a biological sample with a defined amount of an exogenous nucleic acid, hybridizing under stringent conditions, determining the hybridizing nucleic acids and, where appropriate, comparing with a standard; or

b) incubating a biological sample with a pair of oligonucleotide primers with specificity for a PARP homolog-encoding nucleic acid, amplifying the nucleic acid, determining the amplification product and, where

appropriate, comparing with a standard.

25. (previously amended) A method for the qualitative or quantitative determination of a PARP homolog as claimed in claim 1, which comprises
    a) incubating a biological sample with a binding partner specific for a PARP homolog,
    b) detecting the binding partner/PARP complex and, where appropriate,
    c) comparing the result with a standard.

26. (original) A method as claimed in claim 25, wherein the binding partner is an antibody or a binding fragment thereof, which carries a detectable label where appropriate.

27. (original) A method as claimed in claim 24 for diagnosing energy deficit-mediated illnesses.

28. (previously amended) A method for determining the efficacy of PARP effectors, which comprises
    a) incubating a PARP homolog as claimed in claim 1 with an analyte which comprises an effector of a physiological or pathological PARP activity; removing the effector again where appropriate; and
    b) determining the activity of the PARP homolog, where appropriate after adding substrates or cosubstrates.

29. (previously amended) A gene therapy composition, which comprises in a vehicle acceptable for gene therapy a nucleic acid construct which
    a) comprises an antisense nucleic acid against a coding nucleic acid as claimed in claim 6; or
    b) a ribozyme against a nucleic acid as claimed in claim 6; or
    c) codes for a specific PARP inhibitor.

30. (previously amended) A pharmaceutical composition comprising, in a pharmaceutically acceptable vehicle, at least one PARP protein as claimed in claim 1, at least one PARP binding partner or at least one coding nucleotide sequence.

31. (original) The use of low molecular weight PARP binding partners as claimed in claim 5 for the diagnosis or therapy of pathological states in the development and/or progress of which at least one PARP protein, or a polypeptide derived therefrom, is involved.

32. (original) The use of low molecular weight PARP binding partners as claimed in claim 5 for the diagnosis or therapy of pathological states mediated by an energy deficit.